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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/824,829	04/14/2004	Nurith Kurn	492692001300	7311

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EXAMINER

BABIC, CHRISTOPHER M

ART UNIT	PAPER NUMBER
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1637

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06/15/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/824,829	Applicant(s) KURN ET AL.	
	Examiner Christopher M. Babic	Art Unit 1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 2/23/2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) See Continuation Sheet is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) See Continuation Sheet is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of the Claims

Claim(s) 1-7, 24, 27-28, 33-36, 39-40, 46-49, 51-60, 62-65, 67-70, 74-79, 81-101, 104-108, 115-116, 120, 122-123, 127-130, 135-136, 139-140, 146-158, 160-163, 166-182, 185, and 188-200 are pending. The following Office Action is in response to Applicant's response dated February 23, 2007.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following rejection is based on a new ground(s) of rejection.

Claim(s) 189 and 190 are rejected under 35 U.S.C. 102(b) as being anticipated by Cleuziat et al. (U.S. 5,824,517).

With regard to claim(s) 189, Cleuziat teaches a kit comprising a composite primer that is capable of binding to multiple sites within a template polynucleotide (fig. 1; col. 8, lines 40-50; col. 27-28, claim 13, for example). It is submitted that the composite

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primers of Cleuziat, as with any primer, necessarily has virtually an infinite number of possible template nucleic acids that contain multiple primer binding sites capable of hybridizing to the same primer sequence. It is further submitted that the instructions for carrying out the various independent methods of the instant invention does not distinguish the claimed product from the prior art. In a recent court decision, *In re Ngai*, 70 USPQ2d 1862 (Fed. Cir. 2004), the court found that a claim directed to kit for performing method of normalizing and amplifying ribonucleic acids was properly rejected as anticipated by prior art, even though content of instructions in claimed kit differs from instructions in prior art, since addition of new set of instructions into known kit merely teaches new use for existing product, in that instructions do not interrelate with kit so as to produce new product, and since addition of printed matter to existing product will not distinguish invention from prior art in terms of patentability if printed matter is not functionally related to product. The decision cited *In re Gulack*, 217 USPQ 401 (Fed. Cir. 1983), where the court found, "...where the printed matter is not functionally related to the substrate, the printed matter will not distinguish the invention from the prior art in terms of patentability."

With regard to claim(s) 190, Cleuziat teaches auxiliary primers (fig. 1, C1, C2, for example).

Claim Rejections - 35 USC § 103

The rejections of claim(s) 1-42, 46-60, 62-79, 81-103, 105-142, 146-165, 170-176, 177-182, 183, 184, 185, 186, and 188 over Kurn in view of Lizardi have been withdrawn in view of Applicant's amendment.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The following rejection is based on a new ground(s) of rejection.

Claim(s) 84-101, 105-107, 149-158, 160-163, 167-182, 185, 188, 199, and 200 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cleuziat (U.S. U.S. 5,824,517) in view of Kass et al. ("Inter-Alu polymerase chain reaction: advancements and applications" Anal Biochem. 1995 Jul 1;228(2):185-93).

With regard to claim(s) 84, Cleuziat teaches methods of DNA amplification utilizing a composite primer comprising an RNA portion and a 3' DNA portion (fig. 1; col. 11, for example), a DNA and RNA-dependent DNA polymerase (col. 10, lines 10-20; col. 11, lines 20-25, for example), and an agent that cleaves RNA from an RNA/DNA heteroduplex (col. 11, lines 50-60, for example), whereby multiple copies of polynucleotide amplification product are generated by primer extension and strand displacement (fig. 1; col. 11, for example).

With regard to claim(s) 85-88 Cleuziat teaches auxiliary primers (fig. 1, C1, C2, for example).

With regard to claim(s) 89 Cleuziat teaches RNA-dependent DNA polymerase (col. 10, lines 10-20; col. 11, lines 20-25, for example).

With regard to claim(s) 90 and 91, Cleuziat teaches RNase H (col. 11, lines 50-60, for example).

With regard to claim(s) 92-97, Cleuziat teaches the recited enzyme mixtures (col. 5, line 1-30; col. 9-10, for example).

With regard to claim(s) 98-101, Cleuziat teaches composite primers of the recited configurations (example 1, SEQ ID NO: 3,4, for example).

With regard to claim(s) 105-107, Cleuziat teaches modified nucleotides (col. 5, dUTP; col. 14, lines 55-65, labeled nucleotides, for example).

With regard to claim(s) 149-158, 160-163, and 167-169, please refer to the corresponding rejections above.

With regard to claim(s) 170-176, Cleuziat teaches immobilizing amplification products in the under the recited configurations (col. 5, lines 45-65; col. 14, lines 1-55, for example).

With regard to claim(s) 177-182, Cleuziat teaches characterizing amplification products in the under the recited configurations (col. 1, lines 10-40; col. 14-15, for example).

With regard to claim(s) 185, the amplification methods of Cleuziat necessarily create libraries of polynucleotide amplification products (fig. 1; col. 11, for example).

With regard to claim(s) 188, absent of any formal definition of the term "storing", the term is has been interpreted to encompass any amount of time after amplification. Cleuziat teaches the storage of polynucleotide amplification product between amplification and characterization (col. 1, lines 10-40; col. 14-15, for example).

With regard to claim(s) 199 and 200, Cleuziat teaches genomic DNA (col. 8, lines 45-55, for example).

Cleuziat does not expressly teach the hybridization of a composite primer to a multiplicity of template sites, i.e. Cleuziat does not teach the hybridization of a population of identical primer sequences to multiple different sites on one template nucleic acid.

It is submitted that multiplexing amplification reactions, i.e. the amplification of multiple loci of a nucleic template in one reaction, was considered routine practice at the time of invention.

Kass provides a supporting disclosure that teaches the multiplex amplification of multiple loci of a template nucleic acid using primer sequence drawn to Alu repeats (fig. 2; pg. 185, section II, for example). Specifically, Kass teaches that, depending on the orientations of the Alu repeats, one primer pair may be used to amplify multiple different sequences, contained between Alu repeats, on the same template (fig. 2, pg. 190-191, section VI, for example).

Returning to the teachings of Cleuziat, the disclosure teaches that some of the major drawbacks of the PCR method are the running of numerous temperature cycles and the limited selection of heat stable polymerases (col. 2, lines 55-end, for example). Furthermore, Cleuziat expressly teaches their method as an isothermal method (col. 6, lines 30-40, for example).

Thus, in summary, it is submitted that it would have been *prima facie obvious* to a practitioner of ordinary skill in the art at the time of invention to amplify several inter-Alu segments within a template using one primer pair in a multiplex setting using the isothermal amplification methods of Cleuziat to avoid the numerous temperature cycles and the limited selection of heat stable polymerases that accompany PCR. It is submitted that in a multiplex setting, the identical composite primer would hybridize to a multiplicity of different sites within the template nucleic acid.

Double Patenting

Applicant's arguments (see pg. 27-28 of response) with respect to the rejections of claim(s) 1 and 189 over Kurn (U.S. Patent No. 6,692,918 B2) in view of Lizardi, and

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claim(s) 1 and 189 over Kurn (U.S. Patent No. 6,251,639 B2) in view of Lizardi have been fully considered and are persuasive. Thus, the rejections have been withdrawn.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

It is noted that only representative claims will be discussed.

Claim(s) 1-7, 24, 27-28, 33-36, 39-40, 46-49, 51-60, 62-65, 67-70, 74-79, 81-101, 104-108, 115-116, 120, 122-123, 127-130, 135-136, 139-140, 146-158, 160-163, 166-182, 185, and 191-200 is rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim(s) 9 of Kurn et al. (U.S. 6,946,251).

Although the conflicting claims are not identical, they are not patentably distinct from each other because they are both drawn to the same general inventive method that employs a first primer comprising a random sequence and a composite amplification primer comprising a RNA and 3' DNA portion that hybridizes to the second primer extension product. The only significant differences between the two claimed method are that claim(s) 9 of '251 is directed to amplification of RNA and claim(s) 1 of the instant method recites a first primer that is hybridizable to a multiplicity of sites within the template sites.

Applicant's arguments (see pg. 27 of response) have been carefully considered but are not persuasive. First, one of ordinary skill in the art would recognize DNA as an obvious variant species of nucleic acid over RNA that is capable of being amplified by the claimed method of '251. Second, multiplexing amplification reactions, i.e. the amplification of multiple loci of a nucleic template in one reaction, was considered routine practice at the time of invention. Thus, the instant method is obvious over claim(s) 9 of '251.

Prior Art Search

With regard to claim(s) 1-7, 24, 27-28, 33-36, 39-40, 46-49, 51-60, 62-65, 67-70, 74-79, 81-83, 108, 115-116, 120, 122-123, 127-130, 135-136, 139-140, 146-148, and 191-198, the closest prior art is that of Cleuziat and the inventor's prior patent U.S. 6,251,639. While Cleuziat teaches the use of an RNA-DNA composite primer with an RNA target, degrading the RNA portion of the extended composite primer, and binding

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of an RNA or DNA displacement primer to the single-stranded region resulting from said degrading, there is no teaching or suggestion of using another RNA-DNA composite primer as the displacement primer. While the '639 patent teaches use of such a composite primer as a displacement primer with respect to a single-stranded DNA template, there is no teaching or suggestion of further modifying the method for application to a multiplicity of sites along a target DNA in the manner of the instant claims.

With further regard to claim(s) 104 and 166, a sequence search of the pertinent databases revealed no prior art teaching or fairly suggesting the use of primers having the sequences contained in SEQ ID NOs: 1 and 2.

Conclusion

Claim(s) 1-7, 24, 27-28, 33-36, 39-40, 46-49, 51-60, 62-65, 67-70, 74-79, 81-101, 104-108, 115-116, 120, 122-123, 127-130, 135-136, 139-140, 146-158, 160-163, 166-182, 185, and 188-200 are rejected.

No claims are allowed.

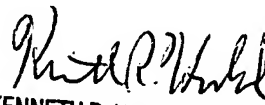
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher M. Babic whose telephone number is 571-272-8507. The examiner can normally be reached on Monday-Friday 7:00AM to 4:00PM.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Christopher M. Babic
Patent Examiner
AU 1637


KENNETH R. HORLICK, PH.D.
PRIMARY EXAMINER
6/7/07

Continuation of Disposition of Claims: Claims pending in the application are 1-7,24,27,28,33-36,39,40,46-49,51-60,62-65,67-70,74-79,81-101,104-108,115,116,120,122,123,127-130,135,136,139,140,146-158,160-163,166-182,185 and 188-200.

Continuation of Disposition of Claims: Claims rejected are 1-7,24,27,28,33-36,39,40,46-49,51-60,62-65,67-70,74-79,81-101,104-108,115,116,120,122,123,127-130,135,136,139,140,146-158,160-163,166-182,185 and 188-200.